General

Guideline Title

Colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis.

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis. London (UK): National Institute for Health and Clinical Excellence (NICE); 2013 Mar. 62 p. (Technology appraisal guidance; no. 276).

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Note for Implementation: The National Institute of Health and Clinical Excellence (NICE) has been made aware that colistimethate sodium dry powder for inhalation is not available at the time of publication of this guidance. NICE is investigating the consequences for the funding direction for this part of the guidance. The guidance and implementation requirements for tobramycin dry powder for inhalation stand as indicated in the "Implementation of the Guideline" field.

Tobramycin dry powder for inhalation (DPI) is recommended as an option for treating chronic pulmonary infection caused by *Pseudomonas aeruginosa* in people with cystic fibrosis only if:

- Nebulised tobramycin is considered an appropriate treatment, that is, when colistimethate sodium is contraindicated, is not tolerated or has not produced an adequate clinical response and
- The manufacturer provides tobramycin DPI with the discount agreed as part of the patient access scheme to primary, secondary and tertiary care in the National Health Service (NHS)

Colistimethate sodium DPI is recommended as an option for treating chronic pulmonary infection caused by *P. aeruginosa* in people with cystic fibrosis only if:

- They would clinically benefit from continued colistimethate sodium but do not tolerate it in its nebulised form and thus tobramycin therapy would otherwise be considered and
- The manufacturer provides colistimethate sodium DPI with the discount agreed as part of the patient access scheme to primary, secondary and tertiary care in the NHS

People currently using tobramycin DPI or colistimethate sodium DPI that is not recommended according to the above paragraphs should be able

to continue treatment until they and their clinician consider it appropriate to stop. For children and young people this decision should be made jointly by the clinician, the child or young person and their parents or carers.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Cystic fibrosis
- Chronic pulmonary infection caused by *Pseudomonas aeruginosa*

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Family Practice

Infectious Diseases

Internal Medicine

Pediatrics

Pulmonary Medicine

Intended Users

Advanced Practice Nurses

Hospitals

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To evaluate the clinical effectiveness and cost-effectiveness of colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis

Target Population

People aged 6 years or older with documented cystic fibrosis who have chronic pulmonary infection caused by *Pseudomonas aeruginosa*

Interventions and Practices Considered

1. Colistimethate sodium dry powder for inhalation (DPI)
2. Tobramycin DPI

Major Outcomes Considered

- Clinical effectiveness
  - Rate and extent of microbial response (e.g., sputum density of *Pseudomonas aeruginosa*)
  - Lung function
  - Respiratory symptoms
  - Frequency and severity of acute exacerbations
  - Health-related quality of life (HRQoL)
  - Adverse events of treatment
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The Assessment Report for this technology appraisal was prepared by the School of Health and Related Research (ScHARR) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Identification of Studies

A comprehensive search was undertaken to systematically identify literature relating to the clinical effectiveness of colistimethate sodium dry powder for inhalation (DPI) and tobramycin DPI for the treatment of *Pseudomonas aeruginosa* in cystic fibrosis. The search strategy comprised the following main elements:

- Searching of electronic databases
- Contact with experts in the field
- Handsearching of bibliographies of retrieved papers

The following electronic databases were searched from inception for published trials and systematic reviews:

- MEDLINE: Ovid. 1950-present
- MEDLINE in-Process and Other Non-Indexed Citations: Ovid. 1950-present
- EMBASE: Ovid. 1980-present
- Cochrane Library: Wiley Interscience
  - Cochrane Database of Systematic Reviews (CDSR). 1996-present
  - Database of Abstracts of Reviews of Effects (DARE). 1995-present

    - Cochrane Central Register of Controlled Trials (CCRT). 1995-present
    - Cochrane Methodology Register. 1904-present
    - Health Technology Assessment Database (HTA). 1995-present
    - National Health Service Economic Evaluation Database (NHS EED). 1995-present
- CINAHL: EBSCO. 1982-present
- Web of Science Citation Index: Web of Knowledge. 1899-present
- Conference Proceedings Citation Index: Web of Knowledge. 1990-present
- BIOSIS Previews: Web of Knowledge. 1969-present

Additional searches were carried out for unpublished studies (e.g., ongoing, completed):

- Agency for Healthcare Research and Quality (AHRQ)
- Bandolier
- Centre for Health Economics (CHE), University of York
- Clinical Trials.gov
- Current Controlled Trials
- The National Research Register Archive: NIHR. 2000-2007
- The MetaRegister of Controlled Trials: Springer Science + Business Media. 2000-present

Manufacturers' submissions received by NICE, as well as any relevant systematic reviews were also handsearched in order to identify any further clinical trials.

The MEDLINE search strategy is presented in Appendix 2 of the Assessment Report (see the "Availability of Companion Documents" field). The search strategy combined freetext and MeSH (Medical subject headings) or thesaurus terms relating to cystic fibrosis, with freetext and MeSH or thesaurus terms relating to *Pseudomonas aeruginosa*, relevant antibiotics and classes of antibiotics and the devices and comparator devices of interest. The search strategy was translated across all databases. No date or language restrictions were applied. Literature searches were conducted during February and March 2011. References were collected in a bibliographic management database, and duplicates removed.

Inclusion and Exclusion Criteria

Inclusion and exclusion criteria were based on the scope provided by NICE. These are set out below.

Inclusion Criteria

Studies were included if they satisfied the following criteria.

Interventions

Studies assessing the effectiveness of colistimethate sodium DPI (used in conjunction with the Turbospin device) or tobramycin DPI (used in conjunction with the TOBI Podhaler device) were included.

Population

Studies including only people aged six years and over with cystic fibrosis and chronic *Pseudomonas aeruginosa* pulmonary infection were selected. Children under six years of age were excluded from the assessment as they are subject to different treatment regimens, methods of assessment of lung function differ, and licensing has not been sought for this age group.

Comparators

Acceptable comparators were: 1) the comparator intervention, or 2) other antipseudomonal antibiotics for nebulised inhalation including as a minimum colistimethate sodium for nebulised inhalation or tobramycin for nebulised inhalation.

Outcomes

Outcomes to be considered by the review were: rate and extent of microbial response (for example sputum density of *Pseudomonas aeruginosa*); lung function; respiratory symptoms; frequency and severity of acute exacerbations; health-related quality of life (HRQoL); and adverse events of treatment (including rate of resistance to antibiotic treatment). Compliance was also considered as a post-hoc addition to the outcomes set out in the NICE scope, as it became evident that this was of relevance to the claims made for the interventions by the manufacturers.

Study Types

Randomised controlled trials (RCTs) were included in the assessment. Data from non-randomised studies were considered, but were not included as evidence was available from RCTs.

Systematic reviews were included if they provided additional data for RCTs meeting the inclusion criteria (that is, unavailable from published trial reports). Other systematic reviews identified were not included but were checked for RCTs that met the inclusion criteria of this review.

Exclusion Criteria

The following were excluded: studies based on animal models; preclinical and biological studies; non RCTs; editorials, opinion pieces; reports published as meeting abstracts only where insufficient details were reported to allow inclusion; studies only published in languages other than English; studies with vasoactive drugs not within their licensed indications; studies in which the population was not restricted to cystic fibrosis, unless data for just this population was presented, and; studies that did not present data for the included outcomes.

Based on the above inclusion/exclusion criteria, study selection was conducted by one reviewer and checked by a second reviewer. In the first instance, titles and abstracts were examined for inclusion. The full manuscripts of citations judged to be potentially relevant were retrieved and further assessed for inclusion.

Scoping searches indicated that a head-to-head trial of the two interventions was unlikely to be available. In anticipation of this, studies which could potentially contribute to a network meta-analysis were also identified on the basis of their abstract and title. Studies were considered potentially useful if they assessed the efficacy of nebulised antibiotics in the target population for the target condition, and reported relevant outcomes. Key study characteristics of the wider network of evidence were extracted by one reviewer. Based on these characteristics, the available network of evidence was constructed. Were viable networks possible, only studies that could contribute to this network would be included in the review. Were a network not possible, only studies providing direct comparisons with at least one intervention and at least one comparator listed in the inclusion criteria were included in the review.

Cost-Effectiveness

Systematic Review of Existing Economic Analyses

Systematic literature searches were undertaken to identify published economic evaluations of colistimethate sodium and tobramycin for the treatment of cystic fibrosis (CF). Details of the search strategies are reported in "Identification of Studies" Section above, and the search strategies for the cost-effectiveness review are presented in Appendix 2 of the Assessment report (see the "Availability of Companion Documents" field). Handsearching of sponsor submissions to NICE was also undertaken in order to identify any further studies missed by the electronic searches. The studies included in the review were critically appraised using the Drummond et al. checklist for economic evaluations.

Three published studies were identified by the systematic searches. None of these three studies relates to either colistimethate sodium or tobramycin in DPI form. However these studies do provide some information concerning the costs and outcomes of the comparator therapies for this assessment and elucidate some of the key methodological problems surrounding the economic evaluation of treatments for CF.

Number of Source Documents

Clinical Effectiveness

Three randomised controlled trials (5 citations) were included in the review.

Cost-Effectiveness

Three economic models were submitted, two by the manufacturers of colistimethate sodium and tobramycin and one by the Assessment Group.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The Assessment Report for this technology appraisal was prepared by the School of Health and Related Research (ScHARR) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Data Extraction and Critical Appraisal Strategy

Data were extracted without blinding either to authors or journal. Data were extracted by one reviewer using a standardised form and checked by a second reviewer. Where multiple publications of the same study were identified, quality assessment and data extraction were based on all relevant publications, and listed as a single study. The quality of included studies was assessed according to three sets of criteria. The purpose of quality assessment was to provide a narrative account of trial quality for the reader, and to inform subgroup analyses (where data allow). In order to assess the risk of bias, items listed in the National Health Service Centre for Reviews and Dissemination (NHS CRD) report were used and were scored as "yes", "no" or "unclear." To assess the clinical relevance and quality of the studies, items were generated from the European medicines Agency (EMA) research recommendations. Two trials were non-inferiority trials; a separate quality assessment form specific to this type of study was also used.

Data Synthesis Methods

The pre-specified outcomes were tabulated and discussed within a descriptive synthesis. Where populations, interventions, outcome measures and available data were comparable and statistical synthesis was considered appropriate, classical meta-analysis or network meta-analysis was planned using Bayesian techniques, or Review Manager® software (The Cochrane Collaboration, version 5.0 http://ims.cochrane.org/revman). If sufficient trials were available, sensitivity analysis was planned to examine whether the removal of poor quality trials influenced the results of the meta-analysis. Consideration was also given to subgroup analyses based on study characteristics.

See Section 5 of the Assessment Report (see the "Availability of Companion Documents" field) for more information on clinical effectiveness analysis.

Cost-Effectiveness

De novo Independent Economic Analysis

The Assessment Group developed a *de novo* health economic model to assess the cost-effectiveness of two competing treatment options (1) colistimethate sodium dry powder inhalation (DPI) versus (2) nebulised tobramycin for the treatment of chronic *Pseudomonas aeruginosa* in patients with cystic fibrosis (CF).

Model Structure

The model estimates the expected costs and quality-adjusted life year (QALY) gains associated with colistimethate sodium DPI versus nebulised tobramycin. The analysis adopts an NHS perspective over a lifetime horizon. The primary economic outcome measure for the analysis is the incremental cost per QALY gained. All costs and health outcomes within the model were discounted using the standard approach at a rate of 3.5%. Costs were valued at 2011 prices.

The model takes the form of a state transition model to estimate transitions between three forced expiratory volume in 1 second (FEV_1) strata ([1] FEV_1 70-99%, [2] FEV_1 40-69%, and [3] FEV_1 <40%). Different levels of health-related quality of life (HRQoL) are assumed for each health state. Treatment duration, which is assumed to be directly related to survival duration, is assumed to be exactly equivalent between the competing treatment options. During each cycle, patients may remain in their current FEV_1 state, transit to an improved or worsened FEV_1 state or die.

Patients with FEV_1<40% may undergo lung transplantation and do not subsequently receive further treatment with colistimethate sodium DPI or tobramycin; other treatments received by these patients are assumed to be identical irrespective of previous antibiotic treatments received. Costs within each treatment group include drug acquisition costs and the costs of managing exacerbations (either in hospital or at home). Potential cost savings associated with reduced maintenance of nebulisers are also included in the economic analysis. Costs associated with follow-up and concomitant medications are assumed to be related only to treatment time and are therefore assumed to be equivalent between treatment groups. A conceptual form of the implemented health economic model is presented in Figure 11 f the Assessment Report (see the "Availability of Companion Documents" field).

Model Validation and Verification Methods

A number of measures were taken to ensure that the Assessment Group model was credible and not subject to computational errors. Firstly, the methods and results of the health economic model were peer reviewed by three clinical advisors to the project. The executable model and its underlying logic were checked by the model authors and a third modeller who was not involved in its development. The expectations of each model parameter were compared against their deterministic counterpart. All model input parameters were double-checked against the sources from which they were derived. The plausibility of the model results were considered against the model developers' expectations of those results prior to model development.

In addition to the above activities, a validation exercise was undertaken to examine the plausibility of the extrapolated Markov trace based on the COLO/DPI/02/06 trial by deriving equivalent transition matrices using longitudinal panel data from the CF Registry for the period 1997-2008. These transition matrices were then applied to the initial distribution of patients in the model and the resulting Markov trace was compared against the Markov trace for the tobramycin group. The results of this analysis are shown in Figure 13 of the Assessment Report (see the "Availability of Companion Documents" field).

See Section 6 of the Assessment Report (see the "Availability of Companion Documents" field) for additional information on cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document

called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions on Cost-Effectiveness

Availability and Nature of Evidence

The manufacturer of colistimethate sodium dry powder for inhalation (DPI) used a cohort-based decision analysis to compare colistimethate sodium DPI with nebulised tobramycin in people aged 6 years or older with documented cystic fibrosis who had chronic pseudomonas lung infection.

The Committee concluded that the manufacturer's model lacked credibility and therefore they would not consider it or its results plausible.

The Committee discussed the Assessment Group's *de novo* model which compared colistimethate sodium DPI with nebulised tobramycin and tobramycin DPI with nebulised tobramycin. The Committee noted that the model had a lifetime time horizon. The Committee agreed that the use of a lifetime horizon was appropriate, but acknowledged the limitation of extrapolating short-term trial results over long time horizons. Additionally the Committee noted other limitations of the Assessment Group model, including the fact that it did not recognise that, in the current treatment pathway, some people would move from one drug to another (for example from colistimethate sodium to tobramycin).

The Committee concluded, however, that despite these limitations the Assessment Group's *de novo* model was the best available framework for assessing the cost-effectiveness of colistimethate sodium DPI compared with nebulised tobramycin and of tobramycin DPI compared with nebulised tobramycin.

The Assessment Group also carried out additional analyses in response to the patient access schemes submitted by the manufacturers of colistimethate sodium DPI and tobramycin DPI.

Uncertainties around and Plausibility of Assumptions and Inputs in the Economic Model

Colistimethate sodium DPI: The Committee had particular concerns about the inconsistent time horizons used in the manufacturer's model for costs and health outcomes and the validity of using mortality benefits associated with 24 weeks of treatment and extrapolating over a lifetime.

The Committee had particular concerns about limitations of the Assessment Group's model. The Committee agreed that the use of a lifetime horizon was appropriate, but acknowledged the limitation of extrapolating short-term trial results over long time horizons. Additionally it noted that the model did not recognise that, in the current treatment pathway, some people would move from one drug to another (for example from colistimethate sodium to tobramycin). The Committee also noted that treatment duration is assumed to be equivalent between the 2 treatments. It agreed that it was also plausible that some people on nebulised tobramycin would receive some form of treatment on a continuous basis (either as continuous nebulised reduced-dose tobramycin or as nebulised colistimethate sodium in off-months from tobramycin) but there was no evidence on which to base any cost-effectiveness estimate.

Tobramycin DPI: The Committee was aware that for the Assessment Group model for tobramycin DPI uncertainty was generated because the analyses were based on the inclusion of aggregate lung disorder data as a proxy measure for exacerbations because data on major and minor exacerbations had not been collected in the EAGER trial.

The quality-adjusted life-year (QALY) gain for tobramycin DPI was uncertain because quality-of-life data were not collected in the EAGER trial.

Incorporation of Health-Related Quality-of-Life Benefits and Utility Values

The Committee discussed the additional benefits of the mode of delivery of the dry powder formulations over nebulised alternatives. The Committee noted that both technologies aimed to give people with cystic fibrosis and chronic *P. aeruginosa* lung infection quality-of-life benefits in terms of ease of use and convenience.

Have Any Potential Significant and Substantial Health-Related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

The Committee acknowledged that the small QALY gain for tobramycin DPI was uncertain because quality-of-life data were not collected in the EAGER trial. However, it agreed it was reasonable to assume that there would be some QALY gain for tobramycin DPI over nebulised tobramycin in clinical practice in view of the reported benefits to patients in terms of ease of use and convenience although it acknowledged that the number of withdrawals from the EAGER trial did not indicate this relationship.

The Committee noted the small QALY loss for colistimethate sodium DPI compared with nebulised tobramycin but also the substantial saving (£38,000 with the list price for nebulised tobramycin). The Committee further observed that adherence might be greater with the use of a dry powder inhaler in such a population.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost-Effective?

Not applicable

What Are the Key Drivers of Cost-Effectiveness?

The key drivers of cost-effectiveness were the cost of interventions and comparators when the most recent patient access schemes were included, and the small QALY gains for tobramycin DPI compared with nebulised tobramycin and for colistimethate sodium compared with nebulised tobramycin.

Most Likely Cost-Effectiveness Estimate (Given as an Incremental Cost-Effectiveness Ratio [ICER])

Tobramycin DPI consistently dominated nebulised tobramycin with inclusion of the patient access scheme, that is, there was a cost saving and QALY gain for tobramycin DPI compared to nebulised tobramycin.

The Committee noted the small QALY loss for colistimethate sodium DPI compared with nebulised tobramycin but also the substantial cost saving (£38,000 with the list price for nebulised tobramycin).

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated for each recommendation.

The Appraisal Committee considered clinical and cost-effectiveness evidence and a review of this evidence by the Evidence Review Group. For clinical effectiveness, three randomised controlled trials were the main source of evidence. For cost-effectiveness, the manufacturers' and the Assessment Group's economic models were considered.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis to delay or slow deterioration in lung function

Potential Harms

- *Colistimethate sodium dry powder inhalation (DPI)*. The summary of product characteristics lists the following adverse reactions for colistimethate sodium DPI: respiratory disorders (such as dyspnoea, cough and wheezing), ear and labyrinth disorders, thoracic and gastrointestinal disorders, musculoskeletal, connective tissue and bone disorders, general disorders and administration site conditions, and renal and urinary disorders.
- *Tobramycin DPI*. The summary of product characteristics lists the following adverse reactions for tobramycin DPI: respiratory, thoracic and mediastinal disorders (such as dyspnoea, productive cough and wheezing), ear and labyrinth disorders, vascular disorders, gastrointestinal disorders, skin and subcutaneous tissue disorders, musculoskeletal, connective tissue and bone disorders, general disorders, and administration site conditions.

For full details of adverse reactions and contraindications, see the summary of product characteristics available at http://emc.medicines.org.uk/ .

Qualifying Statements

Qualifying Statements

- This guidance represents the views of the National Institute for Health and Clinical Excellence (NICE) and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

- The Secretary of State and the Welsh Assembly Minister for Health and Social Services have issued directions to the National Health Service (NHS) in England and Wales on implementing National Institute for Health and Clinical Excellence (NICE) technology appraisal guidance. When a NICE technology appraisal recommends use of a drug or treatment, or other technology, the NHS must usually provide funding and resources for it within 3 months of the guidance being published. If the Department of Health issues a variation to the 3-month funding direction, details will be available on the NICE website. When there is no NICE technology appraisal guidance on a drug, treatment

or other technology, decisions on funding should be made locally.

- The technologies in this appraisal may not be the only treatments for pseudomonas lung infection in cystic fibrosis recommended in NICE guidance, or otherwise available in the NHS. Therefore, if a NICE technology appraisal recommends use of a technology, it is as an option for the treatment of a disease or condition. This means that the technology should be available for a patient who meets the clinical criteria set out in the guidance, subject to the clinical judgement of the treating clinician. The NHS must provide funding and resources (in line with the section above) when the clinician concludes and the patient agrees that the recommended technology is the most appropriate to use, based on a discussion of all available treatments.
- The Department of Health has agreed a patient access scheme with the manufacturer of tobramycin dry powder for inhalation (DPI) (Novartis) that makes tobramycin DPI available to the NHS with a discount on the list price applied to original invoices. The size of the discount is commercial in confidence. It is the responsibility of the manufacturer to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about this patient access scheme should be directed to the manufacturer.
- The Department of Health has agreed a patient access scheme with the manufacturer of colistimethate sodium DPI that makes colistimethate sodium DPI available to the NHS with a discount on the list price applied to original invoices. The size of the discount is commercial in confidence. It is the responsibility of the manufacturer to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about this patient access scheme should be directed to Novartis Pharmaceuticals UK's Commercial Operations Team on 01276 698717 or commercial.team@novartis.com.
- NICE has developed a tool to help organisations put this guidance into practice. This is available on the NICE website (http://guidance.nice.org.uk/ta276).
    - A costing statement explaining the resource impact of this guidance.

Implementation Tools

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis. London (UK): National Institute for Health and Clinical Excellence (NICE); 2013 Mar. 62 p. (Technology appraisal guidance; no. 276).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Mar

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Clinical Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Committee Members: Professor Peter Clark (*Chair*), Consultant Medical Oncologist, Clatterbridge Centre for Oncology; Professor Jonathan Michaels (*Vice Chair*), Professor of Clinical Decision Science, University of Sheffield; Professor Darren Ashcroft, Professor of Pharmacoepidemiology, School of Pharmacy and Pharmaceutical Sciences, University of Manchester; Dr Aomesh Bhatt, Regulatory and Medical Affairs Director Europe and North America, Reckitt Benckiser; Dr Andrew Black, General Practitioner, Mortimer Medical Practice, Herefordshire; Dr Matthew Bradley, Therapy Area Leader, Global Health Outcomes, GlaxoSmithKline; Dr Ian Campbell, Honorary Consultant Physician, Llandough Hospital, Cardiff; Tracey Cole, Lay Member; Dr Ian Davidson, Lecturer in Rehabilitation, University of Manchester; John Dervan, Lay Member; Professor Simon Dixon, Professor of Health Economics, University of Sheffield; Dr Martin Duerden, Assistant Medical Director, Betsi Cadwaladr University Health Board, North Wales; Gillian Ells, Prescribing Advisor – Commissioning, NHS Hastings and Rother and NHS East Sussex Downs and Weald; Dr Jon Fear, Consultant in Public Health Medicine, Head of Healthcare Effectiveness, NHS Leeds; Professor Paula Ghaneh, Professor and Honorary Consultant Surgeon, University of Liverpool; Dr Susan Griffin, Research Fellow, Centre for Health Economics, University of York; Professor John Hutton, Professor of Health Economics, University of York; Professor Peter Jones, Emeritus Professor of Statistics, Keele University; Dr Steven Julious, Reader in Medical Statistics, University of Sheffield; Dr Tim Kinnaird, Lead Interventional Cardiologist, University Hospital of Wales, Cardiff; Rachel Lewis, Advanced Nurse Practitioner, Manchester Business School; Professor Femi Oyebode, Professor of Psychiatry and Consultant Psychiatrist, The National Centre for Mental Health; Dr John Radford, Director of Public Health, Rotherham Primary Care Trust and MBC; Dr Phillip Rutledge, General Practitioner and Consultant in Medicines Management, NHS Lothian; Dr Brian Shine, Consultant Chemical Pathologist, John Radcliffe Hospital, Oxford; Dr Murray Smith, Associate Professor in Social Research in Medicines and Health, University of Nottingham; Paddy Storrie, Lay Member; Professor Carolyn Young, Consultant neurologist, Walton Centre for Neurology and Neurosurgery

Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Clinical Excellence (NICE) Web site .

Availability of Companion Documents

The following are available:

- Colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis. Costing statement. London (UK): National Institute for Health and Clinical Excellence (NICE); 2013 Mar. 5 p. (Technology appraisal; no. 276). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site .
- Colistimethate sodium powder and tobramycin powder for inhalation for the treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis. Technology Assessment Report. Sheffield (UK): School of Health and Related Research (ScHARR), The University of Sheffield. 2012 Mar 13. 216 p. Electronic copies: Available in PDF from the NICE Web site .

Patient Resources

The following is available:

- Colistimethate sodium and tobramycin dry powders for inhalation for pseudomonas lung infection in cystic fibrosis. Information for the public. London (UK): National Institute for Health and Clinical Excellence (NICE); 2013 Mar. 7 p. (Technology appraisal; no. 276). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site .

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